

Washington University Journal of Law & Policy

Volume 44 *Conceptualizing a New Institutional Framework for International Taxation*

2014

Triune Synergy in Biomedical Research: Uniting Pharmaceutical Companies, University Researchers, and the NIH through the Drug Repurposing Project at NCATS

Brian F. Yagi

Washington University School of Law

Follow this and additional works at: https://openscholarship.wustl.edu/law_journal_law_policy



Part of the [Law Commons](#)

Recommended Citation

Brian F. Yagi, *Triune Synergy in Biomedical Research: Uniting Pharmaceutical Companies, University Researchers, and the NIH through the Drug Repurposing Project at NCATS*, 44 WASH. U. J. L. & POL'Y 179 (2014),
https://openscholarship.wustl.edu/law_journal_law_policy/vol44/iss1/14

This Note is brought to you for free and open access by the Law School at Washington University Open Scholarship. It has been accepted for inclusion in Washington University Journal of Law & Policy by an authorized administrator of Washington University Open Scholarship. For more information, please contact digital@wumail.wustl.edu.

Triune Synergy in Biomedical Research: Uniting Pharmaceutical Companies, University Researchers, and the NIH through the Drug Repurposing Project at NCATS

Brian F. Yagi*

I. INTRODUCTION

The drug discovery process is long, expensive, and prone to failure. The average cost of developing an approved drug is increasing exponentially.¹ Exacerbating the problem is the fact that, instead of being translated into medical therapies, basic scientific discoveries are languishing without further development. This phenomenon, known as the “Valley of Death,” has become a concern of the National Institutes of Health (NIH),² which is the main funder of biomedical research in the United States.³ In an attempt to build bridges across the Valley of Death, the NIH created the National Center for Advancing Translational Sciences (NCATS) in December 2011.⁴ NCATS’ first project was the Discovering New Therapeutic Uses for Existing Molecules Program (the “Repurposing Project”).⁵

* J.D. (2014), Washington University in St. Louis School of Law. The author would like to thank Prof. Kevin Emerson Collins for helpful discussion during the drafting process, Dr. Francis Collins for access to and permission to use materials as references in this Note, and the *Journal* editorial staff for their excellent work in editing this Note. All mistakes are my own.

1. See Jack W. Scannell et al., *Diagnosing the Decline in Biomedical R&D Efficiency*, 11 NATURE REV. DRUG DISCOVERY 191, 192 (2012).

2. See Francis S. Collins, *Reengineering Translational Science: The Time is Right*, 3 SCI. TRANSLATIONAL MED. 1, 1 (2011).

3. *About NIH*, NAT’L INST. HEALTH, <http://nih.gov/about/> (last visited Dec. 23, 2013).

4. *NIH Establishes National Center for Advancing Translational Sciences*, NAT’L INST. HEALTH (Dec. 23, 2012), <http://www.nih.gov/news/health/dec2011/od-23.htm> [hereinafter *NIH Establishes*].

5. See Jocelyn Kaiser, *NIH’s Secondhand Shop for Tried-and-Tested Drugs*, 332 SCI. 1492 (2011); Alexander Gaffney, *NCATS’ Development Program Looks to Avoid Regulatory Hurdles for Once-Abandoned Drugs*, REG. FOCUS (June 18, 2013), <https://www.raps.org/focus-online/news/news-article-view/article/3646/>.

The Repurposing Project pairs university researchers with drug candidates owned by pharmaceutical companies that have failed in their first attempts to treat diseases. The university researchers develop and submit proposals to repurpose the drugs to treat different diseases. The NIH then reviews the scientific merits of the project proposals and chooses a group of projects to fund. In the first year of the Repurposing Project, the NIH received over 160 project proposals and chose nine projects to fund in June of 2013.⁶ The NIH intends to continue the Repurposing Project in future years, inviting a new set of university proposals for evaluation.⁷

The linchpin for getting the Repurposing Project off the ground was convincing the pharmaceutical companies to allow outside researchers to experiment with their patented drugs. If an outside researcher were to be successful in finding a new use for the drug, the company's intellectual property (IP) ownership over the drug would be diluted. This, in turn, would limit the company's ability to profit from the drug. In a break from their normally secretive business practices,⁸ the eight participating pharmaceutical companies published Collaborative Research Agreements (CRAs) on the NIH's website that outline the intellectual property rights they were willing to give up in order to participate in the project.⁹

In this Note, I will discuss the content of the CRAs developed for the Repurposing Project. I will examine the IP provisions that each of the eight participating companies incorporated into its CRA. While all of the companies were willing to allow university researchers to

6. *NIH to Fund Collaborations with Industry to Identify New Uses for Existing Compounds*, NAT'L INST. HEALTH (June 18, 2013), <http://www.nih.gov/news/health/jun2013/ncats-18.htm> [hereinafter *NIH to Fund Collaborations*]; Asher Mullard, *An Audience With Chris Austin*, 12 NATURE REV. DRUG DISCOVERY 182, 183 (2013).

7. Christine M. Colvis & Christopher P. Austin, *Innovation in Therapeutics Development at the NCATS*, 39 NEUROPSYCHOPHARMACOLOGY REVS. 230 (forthcoming 2014).

8. See, e.g., Lorraine E. Ferris, *Industry-Sponsored Pharmaceutical Trials and Research Ethics Boards: Are They Cloaked in Too Much Secrecy?*, 166 CAN. MED. ASS'N J. 1279, 1279–80 (2002).

9. The eight participating companies are AbbVie (formally Abbott), AstraZeneca, Bristol-Meyers Squibb Co. ("Bristol"), Eli Lilly & Co. ("Lilly"), GlaxoSmithKline, Janssen Pharmaceutical Research & Development, L.L.C. ("Janssen"), Pfizer, Inc. ("Pfizer"), and Sanofi. See *infra* note 89 and accompanying text.

acquire patents over their discoveries,¹⁰ they were not willing to do so unconditionally. As a result, the CRAs require researchers to give the companies the first opportunity to repurchase these patent rights via a royalty-bearing license. Royalty payments are written into the CRAs and are structured to reward each party for their relative contributions to the project. This scheme enables the drug companies to continue developing these drugs with an eye towards the market and the patients who await the therapies.

In this Note, I will argue that the Repurposing Project aligns the skills and interests of three of the most important entities in biomedical research: universities, drug companies, and the NIH. By bringing these institutions together, NCATS has created an environment in which the three entities can build off of each other's strengths—a triune synergy—that has and will continue to make a positive impact on drug repurposing projects, biomedical research, and global health. Part II of this Note discusses the process of researching and developing pharmaceuticals. It highlights the problem of the Valley of Death and its repercussions in the fields of medicine and public health. It also describes the Repurposing Project proposed by the NIH as a means to help solve those problems.

Part III discusses issues that can arise in partnerships between university researchers and pharmaceutical companies in the area of biomedical research and development, such as concerns over intellectual property. Part IV details the provisions of the CRAs posted by the eight pharmaceutical companies participating in the pilot Repurposing Project. In Part V, this Note analyzes and evaluates the Repurposing Project and the CRAs.

10. *See infra* Part IV.

II. THE REPURPOSING PROJECT AS A BRIDGE ACROSS THE VALLEY OF DEATH

A. The Valley of Death in Biomedical Research and Development

Biomedical research has long been a priority in the United States, with a total of \$119.3 billion spent on the endeavor in 2012 alone.¹¹ The sources of biomedical research funding are diverse; both public and private sources provide funding. The NIH provides the majority of the public funding.¹² Pharmaceutical companies, biotechnology companies,¹³ and nonprofit interest groups contribute much of the private funding.¹⁴ Each funding entity has its own role and objective in pharmaceutical development.¹⁵

In order to develop a therapeutic for a disease, a cellular or molecular target for that disease must be discovered through basic scientific research.¹⁶ The next step is to design a chemical or

11. Justin Chakma et al., *Asia's Ascent—Global Trends in Biomedical R&D Expenditures*, 370 NEW ENG. J. MED. 3, 4 (2014).

12. With the sum of \$27.8 billion, the NIH provided 84 percent of federal funding towards biomedical research in 2007. E. Ray Dorsey et al., *Funding of U.S. Biomedical Research, 2003–2008*, 303 JAMA 137, 139 (2010).

13. A reported \$51.9 billion was spent on biopharmaceutical research in 2007. This represented the largest contribution at 58 percent of total national funding. *Id.* at 138–40.

14. The Health Research Alliance (“HRA”), a consortium of thirty-two private, nonprofit funders of biomedical research, awarded \$1.024 billion in grants in 2008. Elizabeth R. Myers et al., *Similarities and Differences in Philanthropic and Federal Support for Medical Research in the United States: An Analysis of Funding by Nonprofits in 2006–2008*, 87 ACAD. MED. 1574, 1575 (2012) (Table 1). This figure represents approximately 40 percent of total philanthropic health research funding. *Id.* at 1575.

15. Generally speaking, university researchers focus on basic scientific discoveries elucidating causes of disease (and, therefore, the potential targets for drugs). The funding for these projects comes from public dollars, typically from the NIH. Every other step of the process, from preclinical *in vitro* studies through Phase III clinical trials, is traditionally conducted by pharmaceutical companies. *See generally* Ashley J. Stevens et al., *The Role of Public-Sector Research in the Discovery of Drugs and Vaccines*, 364 NEW ENG. J. MED. 535 (2011). As discussed in this Note, the Repurposing Project modifies this paradigm, uniting university researchers and pharmaceutical companies in preclinical and early-phase clinical research.

16. For example, in 1989, researchers discovered that the gene *CFTR* was mutated in cystic fibrosis patients, making it an ideal target for pharmaceutical intervention. John R. Riordan et al., *Identification of the Cystic Fibrosis Gene: Cloning and Characterization of Complementary DNA*, 245 SCI. 1066, 1066, 1071 (1989). The story of seeking a cure for cystic fibrosis through targeting the *CFTR* gene serves as an informative anecdote about the Valley of Death, because in the twenty-four years since the gene's discovery, science has not yet provided

biological molecule that will interact with the disease target.¹⁷ For the purposes of this Note, both small molecule chemicals and biological therapies will be referred to as “drugs.”¹⁸ Once a drug candidate is discovered, it is subtly manipulated to maximize its potential.¹⁹ Next, the lead drug candidate is tested *in vitro* to see if it has the intended mechanistic effects.²⁰ The final preclinical step entails testing the drug in animal models, such as mice and monkeys, to determine if the drug is safe and has any biological effect in the model, non-human organism.²¹ Basic research is traditionally carried out in university laboratories with public funding, and other preclinical steps are usually conducted by pharmaceutical companies.²²

Once all preclinical tests are complete, the drug developer must submit an Investigational New Drug (IND) application to the U.S. Food and Drug Administration (FDA) in order to start clinical

the silver bullet therapy many anticipated. See Helen Pearson, *One Gene, Twenty Years*, 460 NATURE 165, 165 (2009) (reviewing the efforts of the scientific community to discover a cure for cystic fibrosis). The first and only drug targeting *CFTR* was approved in February 2012, but it only works on a rare form of the disease present in 4 percent of the population. Jocelyn Kaiser, *New Cystic Fibrosis Drug Offers Hope, at a Price*, 335 SCI. 645, 645 (2012).

17. See Christopher Lipinski & Andrew Hopkins, *Navigating Chemical Space for Biology and Medicine*, 432 NATURE 855 (2004) (providing an overview of the canonical small molecule drug development paradigm).

18. This definition is appropriate because the library of fifty-eight drugs provided by the pharmaceutical companies for the NCATS Repurposing Project contain both small molecules and biologics. See *infra* note 48.

19. Maximizing the pharmacokinetics while minimizing the toxic effects of the drug at this stage will ostensibly lead to a higher probability of ultimate success. See generally Karen L. Steinmetz & Edward G. Spack, *The Basics of Preclinical Drug Development for Neurodegenerative Disease Indications*, 9 BIOMEDCENTRAL NEUROLOGY 1 (Supp. 2009) (focusing on neurological drugs); James M. Gallo, *Pharmacokinetic/Pharmacodynamic-Driven Drug Development*, 77 MT. SINAI J. MED. 381 (2010) (focusing on cancer drugs).

20. See Lipinski & Hopkins, *supra* note 17, at 857 (discussing the high throughput *in vitro* model of drug development).

21. See *id.* at 855 (discussing different discovery and development paradigms for small molecule and biological drugs); Steinmetz & Spack, *supra* note 19, at 8 (“Definitive animal studies establish the safety characteristics, including the no observable adverse effect level (NOAEL), of the candidate drug. With very few exceptions, these studies are rigorously documented and conducted under regulatory guidelines . . .”).

22. Stevens et al., *supra* note 15, at 535 (“Historically, public-sector researchers have performed the upstream, basic research that elucidated the underlying mechanisms of disease and identified promising points of intervention, whereas corporate researchers have performed the downstream, applied research resulting in the discovery of drugs for the treatment of diseases . . .”).

testing.²³ The FDA will grant an IND only if the preclinical data suggests a favorable benefit versus risk profile.²⁴ Thus, preclinical data carries substantial value in the pharmaceutical industry. Once an IND has been granted, in-human clinical trials can commence.²⁵

Clinical trials usually consist of three phases. During these phases, researchers determine the ideal dosage and patient population for the drug.²⁶ After Phase III, the drug developer can file a New Drug Application (NDA).²⁷ The FDA will approve an NDA if the totality of the data shows a positive risk versus reward profile for the new drug.²⁸ In addition to balancing the risks and rewards of the proposed drug, the FDA also determines which indications the drug will be approved for, and which precautions must be listed on the label.²⁹

This odyssey of development is long (taking an average of thirteen years),³⁰ expensive (costing approximately one billion dollars per approved drug),³¹ and prone to failure (failing more than 95 percent of the time).³² Facing these substantial hurdles, many pharmaceutical companies have moved away from preclinical development,³³ focusing instead on clinical projects for diseases that

23. *Investigational New Drug (IND) Application*, U.S. FOOD DRUG ADMIN., <http://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/investigationalnewdrugindapplication/default.htm> (last visited Feb. 8, 2013).

24. *Id.*

25. *Id.*

26. Phase I clinical trials involve the use of lower, sub-therapeutic doses, and are not intended to research the efficacy of the drug. Instead, the way the body processes the drug (pharmacokinetics) and the drug's toxicity are studied. 21 C.F.R. § 312.21 (2013). In Phase II studies, the dosage is steadily raised to determine which dosage achieves the most favorable balance between therapeutic effect and deleterious side effects. *Id.* Finally, in Phase III trials, the final dose is tested across a large population (hundreds to thousands) for a longer time period to ensure both efficacy and safety. *Id.*

27. *See New Drug Application*, U.S. FOOD DRUG ADMIN., <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/NewDrugApplicationNDA/> (last visited Nov. 5, 2013).

28. *Id.*

29. *Id.*

30. *See* Collins, *supra* note 2.

31. *See* Scannell et al., *supra* note 1.

32. *See* Collins, *supra* note 2, at 3. These metrics are notoriously difficult to calculate with precision because of the diversity of players in the field, the myriad costs that apply across different sectors of the industry, and the multitude ways in which a project can fail. *See also infra* note 38 and accompanying text.

33. John LaMattina, *Universities Stepping Up Efforts to Discover Drugs*, FORBES, Oct. 21, 2013, available at <http://www.forbes.com/sites/johnlamattina/2013/10/21/universities->

are difficult to target but will yield higher profit margins.³⁴ This has created a chasm between preclinical and clinical development such that potential projects based on basic scientific discoveries have failed to advance towards therapeutic development. This abyss is known as the “Valley of Death.”³⁵ Concomitant with (and perhaps because of) the emergence of the Valley of Death, the overall efficiency of biomedical research, as measured by the amount of money it takes to get one new drug approved, has been declining on a logarithmic scale.³⁶ These systemic problems have led to negative consequences for the fields of medicine and human health: of the approximately 4,500 diseases that have a known physiological cause, only 250 have an FDA-approved therapy.³⁷ In an effort to combat these problems, the different players in the field of biomedical

stepping-up-efforts-to-discover-drugs/. Small biotech companies have filled the preclinical void left by larger pharmaceutical companies. Fabio Pammolli et al., *The Productivity Crisis in Pharmaceutical R&D*, 10 NATURE REV. DRUG DISCOVERY 428, 429 (2010). Exacerbating the problem, venture capital firms, which used to be the major source of funding for biotech companies doing preclinical testing, have followed the pharmaceutical companies in avoiding the high-risk preclinical projects. *MoneyTree Report*, PRICEWATERHOUSECOOPERS, <https://www.pwcmoneytree.com/MTPublic/ns/nav.jsp?page=historical> (last visited Feb. 8, 2013) (narrowing search parameters to the biotechnology sector).

34. See Pammolli et al., *supra* note 33, at 431. The authors reviewed the Pharmaceutical Index Database to determine the areas in which pharmaceutical companies have shifted the focus of their research. They found that companies are pursuing difficult targets and that those projects have been decreasing their probability of success. *Id.* at 429, 433. These projects are more costly, as later phase clinical trials are also more expensive. Christopher P. Adams & Van V. Brantner, *Estimating The Cost Of New Drug Development: Is It Really \$802 Million?*, 25 HEALTH AFF. 420, 423 (2006) (showing mean Phase I cost at \$31 million, mean Phase II cost at \$42 million, and mean Phase III cost at \$119 million in year 2000 dollars). Such projects also have higher failure rates. Pammolli et al., *supra* note 33, at 429.

35. The Valley of Death can be conceptualized in multiple ways. The most common way is to put basic research on one side and clinical medicine on the other. Put another way, this puts scientists and doctors on opposite sides of the valley. See generally Declan Butler, *Translational Research: Crossing the Valley of Death*, 453 NATURE 840 (2008) (discussing the historical development of the Valley of Death and one of the early NIH responses—the development of a nationwide network of clinical translational science centers affiliated with major research universities).

36. See Scannell et al., *supra* note 1, at 192. The authors termed this logarithmic decrease “Eroom’s Law,” because it is the exact opposite of Moore’s Law—the logarithmic increase that describes the advances of the technology industry. *Id.* at 191.

37. FRANCIS S. COLLINS, NAT’L INST. OF HEALTH, NIH’S NAT’L CENTER FOR ADVANCING TRANSLATIONAL SCIS. 10 (Apr. 12, 2012) (on file with author).

research and development have attempted to refine their operations with the goal of building bridges across the Valley of Death.³⁸

B. NCATS and the Repurposing Project

In 2003, then-NIH Director Dr. Elias Zerhouni made translational research a priority.³⁹ Translational research is impossible to define with precision because of the myriad scientific procedures that can be classified as “translational.”⁴⁰ However, it can be functionally described as any type of research that is meant to alleviate the problems of the Valley of Death by translating biomedical discoveries into FDA-approved therapies.⁴¹ Dr. Zerhouni’s successor at the NIH, Dr. Francis Collins,⁴² continued the NIH’s commitment to

38. See, e.g., U.S. FOOD & DRUG ADMIN., INNOVATION OR STAGNATION: CHALLENGE & OPPORTUNITY ON THE CRITICAL PATH TO NEW MED. PRODUCTS 5 (2004), available at <http://www.fda.gov/ScienceResearch/SpecialTopics/CriticalPathInitiative/CriticalPathOpportunitiesReports/ucm077262.htm> (concluding, *inter alia*, that the “medical product development process is no longer able to keep pace with basic scientific innovation” and that “[w]e must modernize the critical development path that leads from scientific discovery to the patient”).

39. Elias Zerhouni, *The NIH Roadmap*, 302 SCI. 63, 63 (2003). After consulting with 300 leaders in biomedical research and development and deliberating within NIH-led working groups, the NIH launched a number of new initiatives that fit under the broad umbrella of translational research. *Id.* The stated goals of the roadmap were to “reengineer[] the clinical research enterprise” and to forge “research teams of the future.” *Id.* at 63. The Repurposing Project analyzed in this Note resonates with both of those goals and, therefore, is a prime example of how the NIH has continued to develop its goals in promoting translational science.

40. See, e.g., Butler, *supra* note 35, at 841 (“Ask ten people what translational research means and you’re likely to get ten different answers.”); Collins, *supra* note 2, at 2–4 (describing with specificity ten distinct biomedical translational research projects that could help cross the Valley of Death).

41. “Bench to bedside” is an oft-used descriptor of translational research. Since most biological research is done at a laboratory bench and final treatments are delivered at a patient’s bedside, the phrase is fitting. Butler, *supra* note 35, at 841.

42. Dr. Collins has been an ardent, pragmatic, and hard-working proponent of advancing translational research as NIH Director, for which he has been the recipient of some criticism. Jocelyn Kaiser, *Jeremy Berg: An Independent Scientist Departs NIH’s Ranks*, 332 SCI. 533, 533 (2011). To understand Dr. Collins’ vision as NIH Director, it is important to note that his career has been replete with struggles to traverse the Valley of Death. Earlier in his career, Dr. Collins was among the group of researchers who discovered the *CFTR* gene, for which there have been significant difficulties in developing a pharmaceutical therapy. See Riordan et al., *supra* note 16. Subsequently, Dr. Collins led the Human Genome Project, which has generated an explosion of basic scientific knowledge regarding human biology, but also requires a multitude of translational research to accrue actual medical benefits. See generally Francis S. Collins et al., *The Human Genome Project: Lessons from Large-Scale Biology*, 300 SCI. 286, 289–90

translational research by launching the National Center for Advancing Translational Sciences (NCATS) in December 2011.⁴³ NCATS' mission is to "catalyze the generation of innovative methods and technologies that will enhance the development, testing and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions."⁴⁴

Shortly after its inception, NCATS launched the Repurposing Project.⁴⁵ The Project facilitates research partnerships between pharmaceutical companies and university researchers. Traditionally, pharmaceutical companies have fiercely protected the identity of and preclinical data behind a potential drug candidate.⁴⁶ If a project fails in its first attempt at FDA approval, however, the only way a company can profit from the drug is to repurpose it to treat another disease. The Repurposing Project is meant to unite a university

(2003) (prescribing the future scientific work needed to translate the information gleaned from the Human Genome Project into medical treatments).

43. See *NIH Establishes*, *supra* note 4. The process of creating NCATS began in May 2010, when Dr. Collins requested the Scientific Management Review Board ("SMRB") determine how NIH could better support translational and therapeutic sciences. In December 2010, the SMRB recommended a new translational medicine and therapeutics center be created, and for NIH to conduct an extensive and detailed analysis of what the new center's impact would be. NAT'L INST. HEALTH, REPORT ON TRANSLATIONAL MED. & THERAPEUTICS 2 (Dec. 7, 2010), available at smrb.od.nih.gov/documents/reports/TMAT_122010.pdf. In accordance with that directive, Dr. Collins assembled an NCATS working group and the Advisory Council to the Director on NCATS to brainstorm about specific projects that NCATS could undertake. Francis Collins, *Catalyzing Innovation: The NIH National Center for Advancing Translational Sciences*, PowerPoint presentation delivered at the National Institute of Health (Mar. 14, 2011) (PowerPoint on file with author). It took Congress one year to officially approve NCATS. Consolidated Appropriations Act, 2012, Pub. L. No. 112-74 (2011).

44. *About NCATS*, NAT'L CTR. ADVANCING TRANSLATIONAL SCIS., <http://www.ncats.nih.gov/about/mission.html> (last visited Feb. 8, 2013).

45. See Kaiser, *supra* note 5. NCATS staff spent months planning and coordinating with the participating pharmaceutical companies before the Repurposing Project was launched. On April 21 and 22, 2011, Dr. Collins hosted an NIH-Industry Roundtable for Exploring New Uses for Abandoned and Approved Therapeutics. The purpose was to introduce a model Collaborative Research Agreement, crafted by the NIH's Office of General Counsel (materials, including the draft model agreement, on file with author). The eight participating companies' CRAs that are discussed in this Note were based on that model agreement.

46. See generally F.M. Scherer, *The Political Economy of Patent Policy Reform in the United States* 6-9 (Harvard University School of Government Faculty Working Paper Series RWP07-42, 2007). See also Peter Gwynne & Gary Heebner, *Laboratory Technology Trends: Drug Discovery: 4: Protecting the Assets*, 297 SCI. 2083, 2086 (2002) (quoting Head of Patents, Pharma, and Generics for Novartis: "We pursue all ways of protecting our drug products and take a defensive approach to protecting our research tools.").

researcher, who has an idea for the new disease target, with the pharmaceutical company that has IP rights to the drug.⁴⁷

In 2013, which served as the pilot year for the Project, eight participating pharmaceutical companies posted information about fifty-eight potential drugs on the NCATS website.⁴⁸ Each of the eight companies signed a Memorandum of Understanding (MOU) with the NIH, outlining the goals of the Repurposing Project and the responsibilities of the company.⁴⁹ University researchers then prepared a pre-proposal for a repurposing project based on the posted drug information.⁵⁰ The researchers with the top pre-proposals, as decided through NIH's peer review process, drafted full Project Plans in collaboration with the relevant company.⁵¹ These Project Plans included the specific activities of each party, the transfer of the drug from the company, and specific stop/go criteria that would determine when the project was concluded and whether the company would continue to develop the drug towards FDA approval.⁵² After reviewing the full Project Plans, NCATS chose the most meritorious

47. One way to visualize the project in terms of the Valley of Death is to imagine that pharmaceutical companies hold a large pile of potentially therapeutic molecules on one side of the valley, while university researchers have a mountain of scientific knowledge about the mechanisms that cause disease on the other side of the valley. The purpose of the Repurposing Project is to build a bridge between these two camps to allow collaboration towards clinical development.

48. NAT'L CTR. FOR ADVANCING TRANSLATIONAL SCIS., DISCOVERING NEW THERAPEUTIC USES FOR EXISTING MOLECULES (June 2013), *available at* <http://www.ncats.nih.gov/files/factsheet-therapeutics.pdf>. The information includes, for example, the mechanism of action, safety/tolerability, and the overview of clinical development for each drug, as well as links to clinical trial data (if any) and publications (if any). *Library of Industry-Provided Agents*, NAT'L CTR. FOR ADVANCING TRANSLATIONAL SCIS., <http://www.ncats.nih.gov/research/reengineering/rescue-repurpose/therapeutic-uses/directory.html> (last visited Feb. 8, 2013).

49. C. M. Colvis et al., *Partners for Therapeutic Discovery*, 93 CLINICAL PHARMACOLOGY & THERAPEUTICS 24, 25 (2013). NAT'L CTR. FOR ADVANCING TRANSLATIONAL SCIS., MEMORANDUM OF UNDERSTANDING BETWEEN NAT'L INST. OF HEALTH DEPT. OF HEALTH & HUMAN SERVICES & Co. CONCERNING NIH-INDUS. PROGRAM: DISCOVERING NEW USES FOR EXISTING MOLECULES, *available at* <http://www.ncats.nih.gov/files/MOU-template.pdf> (last visited Feb. 8, 2013) [hereinafter MOU].

50. MOU, *supra* note 49 at 4.

51. *Id.*

52. *Id.* at 4–5.

projects to fund. NCATS received over 160 pre-proposals,⁵³ from which it chose nine projects to initially fund in June of 2013.⁵⁴

As repurposed drugs are eligible for new patents, the Repurposing Project as a whole poses difficulties for the participating pharmaceutical companies. These new method-of-use patents would last longer and therefore be more profitable than the original patents.⁵⁵ Since only inventors are vested with the property rights of their inventions, theoretically, pharmaceutical companies involved in the Repurposing Project risk losing their patent protection to the university researcher if the drug turns out to be useful for its new purpose.⁵⁶ Thus, to ensure this risk is properly offset by the potential benefits, each company involved in the Repurposing Project crafts a model Collaborative Research Agreement (“CRA”), which each researcher must sign before beginning the project.⁵⁷

53. Mullard, *supra* note 6, at 183.

54. *NIH to Fund Collaborations*, *supra* note 6.

55. These new patents would be method-of-use patents, which provide rights to the drug only when used in the course of the particular treatment. See *Manual of Patent Examining and Procedure* § 2106.01 2100-1, 2100-20 (2012) (“A claim with steps that add something of significance to the natural laws themselves would be eligible because it would confine its reach to particular patent-eligible applications of those laws, such as a typical patent on a new drug (including associated method claims) or a new way of using an existing drug.”) (emphasis added).

56. “Conception is the touchstone of inventorship . . .” *Burroughs Wellcome Co. v. Barr Labs., Inc.*, 40 F.3d 1223, 1227 (Fed. Cir. 1994). “Conception is complete when one of ordinary skill in the art could construct the apparatus without unduly extensive research or experimentation.” *Sewall v. Walters*, 21 F.3d 411, 415 (Fed. Cir. 1994). Based on those two definitions, the university researcher will inevitably be either the sole inventor or joint-inventor of any method-of-use patent that arises through the Repurposing Project. Thus, if the pharmaceutical company wants to maintain complete ownership over the IP rights of the project, it must force the researcher to assign his/her rights to the company or buy back a license from the research university. See *infra* notes 107–12 and accompanying text.

57. Each company uploaded its template agreement available for download from the NCATS website. See generally *Template Agreements*, NAT’L CTR. ADVANCING TRANSLATIONAL SCIS., <http://www.ncats.nih.gov/research/reengineering/rescue-repurpose/therapeutic-uses/agreements.html> (last visited Nov. 5, 2013). It would be difficult for university researchers to lawfully obtain the research drug without first obtaining a license from the company through an agreement like a CRA. Although a researcher at a public university can invoke sovereign immunity in defense of an infringement action, and therefore can, in theory, infringe with impunity, such a situation is unlikely in practice. RICHARD S. GRUNER ET AL., *TRANSACTIONAL INTELLECTUAL PROPERTY: FROM STARTUPS TO PUBLIC COMPANIES* 893–94 (2012). Most companies ask public universities to waive their right to invoke sovereign immunity in defense of an infringement suit when they sign a partnership agreement. *Id.* Alternatively, a university researcher could try to experiment with the drug without the drug

III. CONCERNS THAT ARISE DURING BIOMEDICAL RESEARCH COLLABORATIONS BETWEEN UNIVERSITIES AND PHARMACEUTICAL COMPANIES

Two major points of friction arise between universities and companies participating in the Repurposing Project: Who is entitled to control the future arising IP? And how should the costs, risks, and rewards be allocated amongst the participants? In this section, these questions will be analyzed from the perspectives of the university participant, the private pharmaceutical company, and the patients who await the fruits of biomedical research.⁵⁸ A well-designed collaborative project should create synergies between the participants' skills and goals that will drive innovation in drug repurposing research.

A. Future Arising Intellectual Property

The Bayh-Dole Act of 1980 allows recipients of federal grants to keep the IP rights to inventions arising from those publicly-funded research projects.⁵⁹ This resulted in an explosion of university-owned

company's permission following the ruling in *Merck KGAA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 208 (2005). In *Merck*, the Supreme Court broadly interpreted the 35 U.S.C. § 271(e)(1) experimental use exception to infringement. If an experimenter has a "reasonable basis for believing that the experiments will produce the types of information that are relevant to an IND or NDA," he can use a patented drug in that experiment without the patent holder's permission. *Id.* at 208 (internal quotations omitted). In practice, however, a researcher would need more than just the physical drug to do an effective repurposing experiment. He would also need supplemental information, such as how to make and use the drug in experiments. This know-how is likely protected as confidential information by the company. Additionally, in order to apply for an IND, the researcher will need to submit preliminary safety and toxicology data. These are also confidential trade secrets. Aaron S. Kesselheim & Michelle M. Mello, *Confidentiality Laws and Secrecy in Medical Research: Improving Public Access to Data on Drug Safety*, 26 HEALTH AFF. 483, 483 (2007).

58. Because of its mission to "seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability," the NIH will serve as a proxy for patients awaiting cures and the enterprise of biomedical research as a whole for the purposes of discussing policy interests in this Note. *About NIH: Mission*, NAT'L INST. HEALTH, <http://www.nih.gov/about/mission.htm> (last visited Feb. 8, 2013).

59. Bayh-Dole Act of 1980, Pub. L. No. 96-517, 6(a), 94 Stat. 3015, 3019-28 (1980) (codified as amended at 35 U.S.C. 200-212 (1994)).

patents.⁶⁰ Since universities traditionally focus on basic research and generally do not have the capacity to manufacture pharmaceuticals,⁶¹ they often license their patented discoveries to private companies that are built to drive projects through clinical development.⁶² In this traditional paradigm, universities and pharmaceutical companies operate at arms-length. Universities' technology transfer offices bring in substantial revenue to their institutions through licensing patented inventions.⁶³ Thus, in a biomedical research partnership, the university typically prefers to be the owner (or co-owner) of future arising patents so it can generate revenue through licensing agreements.⁶⁴

60. Arti K. Rai & Rebecca S. Eisenberg, *Bayh-Dole Reform and the Progress of Biomedicine*, 66 LAW & CONTEMP. PROBS. 289, 291–92 (2003). The goal of the Bayh-Dole Act was to spur further development of basic research discoveries by extending intellectual property protection to those discoveries. 35 U.S.C. 200 (2006) (stating that the purpose of the Bayh-Dole Act is to “use the patent system to promote the utilization of inventions arising from federally funded research or development . . .”). With the basic research guarded by a patent, a private pharmaceutical company would only be willing to buy a license to use that patent if it could be assured a reasonable return on investment through developing the product to gain FDA approval.

61. See Stevens et al., *supra* note 15.

62. See, e.g., *Wisconsin Alumni Research Found. v. Xenon Pharm., Inc.*, 591 F.3d 876 (7th Cir. 2010). See also Lori Pressman et al., *The Licensing of DNA Patents by US Academic Institutions: An Empirical Survey*, 24 NATURE BIOTECH. 31, 31 (2006).

63. In 2011 alone, licensing revenues from technology transfer offices totaled at least \$2.5 billion. ASS'N UNIV. TECH. MANAGERS, AUTM LICENSING ACTIVITIES SURVEY HIGHLIGHTS 3 (2011), available at http://www.autm.net/AM/Template.cfm?Section=FY_2011_Licensing_Activity_Survey&Template=/CM/ContentDisplay.cfm&ContentID=8731.

64. In *Bd. of Trs. of the Leland Stanford Jr. Univ. v. Roche Molecular Systems, Inc.*, researchers employed at Stanford University collaborated with a private company to learn about a scientific method called PCR. 583 F.3d 832 (Fed. Cir. 2009). The contract between Stanford and the company stated that the researchers would assign any patent rights that the researchers “may devise as a consequence of his work at [the company]” to the company. *Id.* at 837 (internal quotations omitted). Subsequently, the researchers developed a diagnostic test based on PCR to determine the amount of HIV virus in a patient’s blood. *Id.* This research and development was funded by an NIH grant while conducted at Stanford, but was also done at the private company in collaboration with the company’s employed researchers. Stanford applied for and obtained several patents pursuant to the Bayh-Dole Act. *Id.* at 838. Since universities, as opposed to individual researchers, are the recipients of the NIH grant money, Stanford University was the assignee of the patent that issued. When Stanford discovered that the private company had continued to develop its PCR-based HIV detection products, it brought suit for infringement. The Federal Circuit ruled that the agreement between the researcher and the company to assign any future patent rights trumped the default assignment of the patents to Stanford. *Id.* at 844. This case is an illustration of the intellectual property struggles that can arise around owning the patent of a method developed during collaborations between university researchers and private companies.

Unlike universities, pharmaceutical companies focus on drug manufacturing, marketing, and sales to generate profits.⁶⁵ To do so, companies need to either own the patent or buy a license for the IP underlying a particular drug.⁶⁶ Being a licensee rather than a licensor is not an entirely unattractive proposition, as licensees may be able to avoid patent maintenance and litigation costs.⁶⁷ Therefore, so long as the pharmaceutical company has the legal authority to make and use the drug, it does not matter who owns the patent in order for a company to make its profit.⁶⁸ In the context of the Repurposing Project, this flexibility permits companies to forge CRAs that can accommodate a university's desire to acquire patent ownership over inventions that arise during the collaboration,⁶⁹ thereby aligning interests.

Patients awaiting new therapies are best served by having pragmatic repurposing projects commenced as quickly as possible.⁷⁰ Thus, from a policy perspective, it is not important who owns the future arising intellectual patent, so long as both the pharmaceutical

65. See Stevens et al., *supra* note 15.

66. See Rebecca S. Eisenberg, *Pharmaceutical Development and Cost: An American Dilemma: The Problem of New Uses*, 5 YALE J. HEALTH POL'Y L. & ETHICS 717, 721 (2005) ("[P]atents on tangible products (such as drugs) and processes (such as methods of treatment) might motivate firms to invest in data production in order to develop markets for their inventions.").

67. Each patent applicant has to pay \$330 upon submission, pursuant to 35 U.S.C. § 41(a)(1)(A) (2012), and \$220 in examination fees, pursuant to 35 U.S.C. § 41(a)(3)(A)(i). If the patent is approved, the applicant must pay \$1,510 for an issue fee. *Id.* § 41(a)(4)(A). If the applicant wants the patent to remain enforceable for its entire twenty-year window, he or she must pay \$980, \$2,480, and \$4,110 at interim periods. *Id.* § 41(b)(1)(A)-(C). The grand total comes to \$9,660. A 2011 survey indicates that litigation costs for patent-related claims in which the amount in controversy was greater than \$25 million averages \$3 million at the end of discovery and \$5 million at the end of trial. Jim Kerstetter, *How Much is That Patent Lawsuit Going to Cost You?*, CNET (Apr. 5, 2012), http://news.cnet.com/8301-32973_3-57409792-296/how-much-is-that-patent-lawsuit-going-to-cost-you/.

68. Benjamin N. Roin, *Unpatentable Drugs and the Standards of Patentability*, 87 TEX. L. REV. 503, 513 (2009) ("Not surprisingly, firms in the [pharmaceutical] industry consistently report that patent protection is essential to their efforts to discover and develop new drugs. Moreover, it is well known that pharmaceutical companies generally refuse to develop new drugs unless they have strong patent protection over them.").

69. See *supra* notes 60–64 and accompanying text.

70. Meredith Wadman, *NIH Director Wins Bid for Translational Medicine Center*, NATURE (Dec. 8, 2010), <http://www.nature.com/news/2010/101208/full/news.2010.650.html> (pointing out that Congress too has pushed to "speed therapies to the bedside, as new drug pipelines at pharmaceutical companies have languished").

company and the university researcher reach an agreement ex-ante that facilitates the project.⁷¹ This normative approach may seem to suggest that CRAs and licenses should be negotiated on a project-by-project basis. Research has shown, however, that having standardized templates for these contracts leads to quicker agreements and, therefore, increases social welfare.⁷² Thus, the NCATS Repurposing Project was bolstered by the fact that pharmaceutical companies were willing to post their template CRAs online as a starting point for determining where they stood on issues surrounding intellectual property rights.

B. The Costs and Benefits of Repurposing Projects

A drug repurposing project that culminates in FDA approval can lead to an extremely lucrative pharmaceutical. Indeed, the blockbuster Viagra is a repurposed drug. Viagra was originally intended to treat angina and hypertension,⁷³ but the Phase I clinical trials showed only marginal efficacy. The drug was repurposed to treat erectile dysfunction, and FDA approval was granted.⁷⁴ In 2010 alone, Viagra sales for Pfizer totaled \$1.928 billion.⁷⁵

Pharmaceutical companies must carefully choose which drug candidates to include in a repurposing project to maximize potential

71. See generally Roin, *supra* note 68.

72. See Marcel Kahan & Michael Klausner, *Standardization and Innovation in Corporate Contracting*, 83 VA. L. REV. 713, 730–33 (1997) (showing that standardized contracts can create positive externalities that drive efficiency in forging collaborations). Starting with a template gives the university an understanding of what terms are acceptable to the pharmaceutical company, decreasing negotiation time in crafting a contract. Thus, the Repurposing Projects will launch sooner with the templates in place than in a world where the parties would have to negotiate *de novo*. This, on a macro scale, means that the research projects funded by NCATS will start sooner, which is beneficial to both the scientific community and to patients awaiting the fruits of the research.

73. CASE STUDIES IN DRUG RESCUE & REPURPOSING, NIH-INDUS. ROUNDTABLE: EXPLORING NEW USES FOR ABANDONED & APPROVED THERAPEUTICS 39 (2011) (on file with author) [hereinafter CASE STUDIES].

74. Many of the male research subjects in the first trial reported unsolicited and irrepressible erections, prompting researchers to repurpose the drug for erectile dysfunction. *Id.*

75. SEC. & EXCH. COMM'N, PFIZER INC. 2010 ANNUAL REPORT 25, available at <http://www.sec.gov/Archives/edgar/data/78003/000119312511048877/dex13.htm> (last visited Feb. 8, 2013).

profits.⁷⁶ For the pilot Repurposing Project, the eight companies chose drugs that were not FDA-approved for their originally intended purpose.⁷⁷ This enabled the companies to maximize the time it could exclude a generic competitor from the market, thereby maximizing its profit potential profitability.⁷⁸

For any repurposing project, however, a series of costs and potential risks stand in the way of realizing the profits of a successfully repurposed drug like Viagra.⁷⁹ A goal of the NCATS

76. The companies have to be sure that the drug has not yet been patented for the process of treating any new disease that would be proposed in the NCATS project. *See supra* note 55 and accompanying text. A new method-of-use patent would allow the company to exclude generic makers from the market for twenty years from the issue of the new method patent. *See Eisenberg, supra* note 66, at 721 (“Data from clinical trials of new uses might expand the market for drugs, and patents on drugs and methods of use might be used to exclude free riders from competing for these sales during the patent term.”).

77. Drug companies sometimes seek to gain FDA approval for the treatment of additional diseases after gaining approval for the first. For example, Avastin was originally approved to treat metastatic colon and rectal cancer in 2004. In an effort to reach more patients, Avastin’s maker, Genentech, launched clinical trials to gain approval for the treatment of metastatic breast cancer. Mikkael A. Sekeres, *The Avastin Story*, 365 *NEW ENG. J. MED.* 1454, 1454 (2011). The drug was approved to treat breast cancer in 2008. However, after subsequent long-term research, it was determined that Avastin did not confer any benefit to breast cancer patients while exposing them to its potent side effects. *Id.* The FDA revoked its approval for the treatment of breast cancer. *Id.* To determine if the fifty-eight drugs available for the NCATS Repurposing Project had previously attained FDA approval for another indication, the author searched the FDA Approved Drug Products Database. *Drugs at FDA*, U.S. FOOD DRUG ADMIN., http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Search_Drug_Name (last visited Feb. 8, 2013). As of Feb. 8, 2013, the author determined that none of the fifty-eight drugs had been approved by the FDA for the treatment of any disease.

78. When a generic manufacturer applies for FDA approval, it needs to certify that it is not infringing any patents on the original drug. *See generally* Arti Rai, *Use Patents, Carve-Outs, and Incentives—A New Battle in the Drug-Patent Wars*, 367 *NEW ENG. J. MED.* 491 (2012). Since method-of-use patents often extend beyond the life of the composition of matter patent for a drug (because the method of treatment is discovered after the drug molecule itself), the FDA allows generic manufacturers to continue producing and selling the generic version of the drug after the composition of matter patent has expired. But in order to do so, it must “carve out” the indication covered by the original company’s method-of-use patent. *Id.* This “carve-out” option for generics is limited to scenarios where the brand drug is FDA-approved for an additional indication beyond the oldest method patent covering the drug. The drug companies in this NCATS Drug Repurposing Project have avoided that problem. If the Repurposing Project does culminate in an FDA approval for the new disease, the drug will be protected by the new method of use patent that arises from the project. Thus, a generic will be entirely unable to launch until that new patent expires (after twenty years), giving the pharmaceutical company longer market exclusivity than in the traditional drug development paradigm.

79. For example, the cost of bringing that repurposed drug through the FDA’s rigorous regulatory procedure is a future cost that looms in the background of a repurposing project. *See Adams & Brantner, supra* note 34 and accompanying text.

Repurposing Project is to spread the costs and risks among the pharmaceutical company, the university researcher, and the NIH. These costs and risks should also be adequately offset by future potential profits.⁸⁰

The NIH provides the funding for the research described in a CRA.⁸¹ That Project, however, is not intended to be the end of the drug's development. Clinical trials and FDA approval are the ultimate goal, and reaching this goal can be quite costly. Each phase of clinical development becomes increasingly expensive as the size of each clinical trial increases.⁸² This successive increase in cost is exacerbated by an unpredictable chance of failure at any point in the development pipeline.⁸³ Traditionally, pharmaceutical companies shoulder this substantial risk. Since the NCATS Repurposing Project constitutes just one step in the development process, there must be a point at which the Project is handed back to the pharmaceutical company, which has the manufacturing capacity to take the drug all the way through the FDA-approval process. Once the Project is handed back to the company, it alone shoulders the financial costs of developing the drug.

The individual particularities of each drug in the Repurposing Project leave open the possibility that future CRAs will be negotiated on an individual basis. This approach was used in prior research partnerships and was criticized as promoting gridlock.⁸⁴ One proposal

80. Janice M. Mueller proposed a reach-through royalty system, which provides royalties based on a percentage of sales of an approved product. *No "Dilettante Affair": Rethinking the Experimental Use Exception to Patent Infringement for Biomedical Research Tools*, 76 WASH. L. REV. 1, 65 (2001). This proposal addressed issues with patented upstream research tools as opposed to drug repurposing projects. *Id.* at 1. However, as the CRAs from this project show, *infra* notes 107–12 and accompanying text, these royalty structures represent a possible mechanism of distributing cash rewards based on the allocation of costs and risks between the university researcher and pharmaceutical company.

81. *See infra* note 97 and accompanying text.

82. *See supra* note 34.

83. Phase II success rates are the lowest of any phase and are estimated at between 18 percent and 28 percent. John Arrowsmith, *Phase II Failures: 2008–2010*, 10 NATURE REV. DRUG DISCOVERY 1, 1 (2011). Phase III success rates are estimated at 50 percent. John Arrowsmith, *Phase III and Submission Failures: 2007–2010*, 10 NATURE REV. DRUG DISCOVERY 1, 1 (2011).

84. *See, e.g.*, Christopher A. Lipinski, *The Anti-Intellectual Effects of Intellectual Property*, 10 CURRENT OPINIONS CHEM. BIOLOGY 380 (2006) (elucidating the philosophical differences in medicinal chemistry requirements between the pharmaceutical industry and

to drive more efficient collaborations between pharmaceutical companies, holding large libraries of small-molecule drugs, and university researchers, who can design assays on a disease target, was promoted by Arti Rai et al. in 2008.⁸⁵ The cornerstone of this proposal was for a third party honest broker to conduct high throughput screening assays to determine promising matches between a drug and a target.⁸⁶ Once a successful hit was established, the university researcher interested in the target could negotiate the terms of a license or a CRA with the pharmaceutical company.⁸⁷ This second stage is similar in structure to the NCATS Repurposing Project; however, the Repurposing Project utilizes CRAs with a standardized agreement, analyzed below.⁸⁸

academia that hinders IP negotiations). A broad survey of academia revealed that negotiations between other academic institutions went relatively smoothly. John P. Walsh et al., *Where Excludability Matters: Material Versus Intellectual Property in Academic Biomedical Research*, 36 RES. POL'Y 1184, 1184–91 (2007). However, attempts to acquire a tangible research input was significantly more likely to fail between a university researcher and a pharmaceutical company than between two university researchers. *Id.* at 1191.

85. Arti K. Rai et al., *Pathways Across the Valley of Death: Novel Intellectual Property Strategies for Accelerated Drug Discoveries*, 8 YALE J. HEALTH POL'Y L. & ETHICS 1 (2008).

86. *Id.* at 21–25. While the proposed project was operating in the first-tier “veil of ignorance” stage, the drugs could be used by the third party honest broker based on standardized licensing agreements common to all pharmaceutical companies. Only if a promising lead was discovered would the drug be un-blinded, and negotiations for a collaboration agreement would ensue between the university researcher and pharmaceutical company.

87. “Because the terms of such second-tier partnerships are likely to vary quite substantially depending on the type of target at issue, we do not propose standard-form agreements for this tier.” *Id.* at 25.

88. Rai et al. agreed that standardized agreements were important for efficiently and quickly starting the research project. *Id.* at 12. The authors, however, envision that stage of collaboration as a different scientific experiment than what is actually happening at NCATS. Instead of the third party conducting the high throughput screen to identify matches between drugs and targets, NCATS has already narrowed the targets and mechanisms of action for which each of the fifty-eight drugs will be used. See *Clarification for the NIH-Industry Pilot Program: Discovering New Therapeutic Uses for Existing Molecules PAR-12-203 (X02) Pre-Application, & Limited Competition RFA-TR-12-004 (UH2/UH3) & RFA-TR-12-005 (UH3)*, NAT'L CTR. ADVANCING TRANSLATIONAL SCI. (July 20, 2012), <http://grants.nih.gov/grants/guide/notice-files/NOT-TR-12-008.html> (“[A]pplications that are not proposing studies investigating one of the Agents or targets/mechanisms of action listed on the NCATS website . . . will not be responsive and will not be accepted for review. Compounds must be used in their current formulation. New formulations will not be responsive.”). Compared to the Rai et al. proposal, the Repurposing Project has foregone the first tier of the proposal and moved on to the second tier. Moreover, the drugs in the Repurposing Project have already completed preclinical screening and even early-phase clinical work. Thus, the collaborations forged by

IV. CONTENT OF THE CRAS

The standardized CRAs begin by laying out the governance structures that will oversee the particular project. A Performance Assessment Committee (“PAC”) comprised of two representatives from the company and two from the research institution is charged with reviewing the progress of the project and deciding whether or not to file for a patent on any discoveries, as well as aligning and communicating with the Steering Committee (“SC”).⁸⁹ The SC consists of the principal university researcher, the director of the program from the company, and NIH oversight personnel, including the NIH Project Scientist and NIH Program Official.⁹⁰ The SC is the ultimate decision-making committee, as it decides whether the

these CRAs promote research further down the developmental pipeline than envisioned by Rai et al.

89. See generally Collaborative Research Agreement between Abbot Laboratories (the Company) and [Academic Medical Center] § 4.1, *available at* <http://www.ncats.nih.gov/files/CRA-Abbott.pdf> (last visited Dec. 5, 2013) [hereinafter AbbVie CRA]; Collaborative Research Agreement between AstraZeneca AB (the Company) and [Academic Medical Center] § 4.1, *available at* <http://www.ncats.nih.gov/files/CRA-AZ.pdf> (last visited Dec. 5, 2013) [hereinafter AstraZeneca CRA]; Collaborative Research Agreement between Bristol-Myers Squibb Company (the “Company”) and [Academic Medical Center] § 4.1, *available at* <http://www.ncats.nih.gov/files/CRA-BMS.pdf> (last visited Dec. 5, 2013) [hereinafter Bristol CRA]; Collaborative Research Agreement between GlaxoSmithKline, LLC and [Academic Medical Center] § 4.1, *available at* <http://www.ncats.nih.gov/files/CRA-GSK.pdf> (last visited Dec. 5, 2013) [hereinafter GlaxoSmithKline CRA]; Collaborative Research Agreement between Janssen Pharmaceutical Research & Development, L.L.C. (the Company) and Academic Medical Center § 4.1, *available at* <http://www.ncats.nih.gov/files/CRA-Janssen.pdf> (last visited Dec. 5, 2013) [hereinafter Janssen CRA]; Collaborative Research Agreement between Pfizer Inc. and [Academic Medical Center] § 4.1, *available at* <http://www.ncats.nih.gov/files/CRA-Pfizer.pdf> (last visited Dec. 5, 2013) [hereinafter Pfizer CRA]; Collaborative Research Agreement between Sanofi-Aventis U.S. Inc. and [Academic Medical Center] § 4.1, *available at* <http://www.ncats.nih.gov/files/CRA-Sanofi.pdf> (last visited Dec. 5, 2013) [hereinafter Sanofi CRA]. Eli Lilly’s CRA does not reference a PAC, and the only reference to a steering committee is found in § 4.5: “Consistent with its role as an advisory non-sponsor, Lilly shall be a non-voting member of the Steering Committee.” Collaborative Research Agreement between Eli Lilly and Company and [Academic Medical Center] § 4.5, *available at* <http://www.ncats.nih.gov/files/CRA-Lilly.pdf> (last visited Dec. 5, 2013) [hereinafter Lilly CRA].

90. See AbbVie CRA, *supra* note 89, § 4.1.7.1; AstraZeneca CRA, *supra* note 89, § 4.1.7.1; Bristol CRA, *supra* note 89, § 4.1.7.1; GlaxoSmithKline CRA, *supra* note 89, § 4.1.7.1; Janssen CRA, *supra* note 89, § 4.1.7.1. Pfizer and Sanofi remain silent on the composition of the Steering Committee, ostensibly leaving it to the discretion of the NIH. They do, however, acknowledge that the PAC will “align and communicate with the steering committee of the NIH Grant.” See Pfizer CRA, *supra* note 89, § 4.1.6; Sanofi CRA, *supra* note 89, § 4.1.6.

stop/go criteria described in the Project Plan have been met. It is also charged with ensuring timely publication of all research results (including negative results).⁹¹

The next section in the CRA assigns responsibilities to the company, the researcher, and the NIH. The company provides the research drug,⁹² any required background knowledge, and previously acquired data that would support an IND application.⁹³ Generally, these data are and will remain confidential.⁹⁴ The researcher is responsible for sponsoring any clinical trials, filing the IND with the FDA, and gaining Institutional Review Board approval of the research protocol.⁹⁵ Additionally, under the CRA, the researcher must submit progress reports to the SC so it can monitor progress of the project in accordance with the NIH grant.⁹⁶ The NIH's main role is to

91. *Supra* note 90. The publication of research results can become contentious. University researchers need to publish in peer-reviewed journals to increase their academic reputation and their chance of attaining tenure. Neal S. Young et al., *Why Current Publication Practices May Distort Science*, 5 PLOS MED. 1418, 1420 (2008). The researcher's desire to publish can conflict with private pharmaceutical companies' goals in three situations. First, if the company wants to keep the research results as a trade secret, it cannot be published. *See* NAT'L CONFERENCE OF COMM'RS OF UNIF. STATE LAWS, UNIF. TRADE SECRETS ACT 5 (Approved Draft 1985), available at http://www.uniformlaws.org/shared/docs/trade%20secrets/utsa_final_85.pdf. Second, if the results will lead to a patent application, companies will want to file their patent applications before the publication is submitted. *See* Gwynne & Heebner, *supra* note 46, at 2084 ("Once the patent application is on file, disclosure will not jeopardize the applicant's ability to obtain the patent."). Finally, if the results of the research are unfavorable, the company will not want that information disclosed to the public or to its competitors. For an egregious example of this, see Drummond Rennie, *Thyroid Storm*, 277 J. AM. MED. ASS'N 1238 (1997). The CRAs acknowledge the importance of publication to the researcher. Before publishing, however, the researcher must submit the manuscript to the company. The company can make changes to the manuscript if it discloses confidential information belonging to the company. Additionally, the company can ask the researcher to delay publication for thirty days so it can file a patent covering the information disclosed in the manuscript. *See, e.g.*, AbbVie CRA, *supra* note 89, § 11.

92. *See, e.g.*, AstraZeneca CRA, *supra* note 89, § 6.1.

93. The Memorandum of Understanding each company signed with the NIH provides that it will give the researcher data regarding the drug that would be included in "regulatory data packages," including data for "inclusion in an Investigational New Drug (IND) application," as well as "appropriate research and drug development expertise and enabling technologies" for the drug. *Template Agreements*, *supra* note 57, § A(2)(e) (internal quotations omitted). Furthermore, the company will provide "[p]harmacokinetics data analysis, pharmacokinetics modeling to calculate bioequivalence and drug exposure data, and biomarker . . . [p]rocedures." *Id.*

94. *See, e.g.*, Bristol CRA, *supra* note 89, § 7.1.

95. *See, e.g.*, GlaxoSmithKline CRA, *supra* note 89, § 5.41.

96. *See, e.g., id.* § 5.1.

provide funding for the research outlined in the Project Plan.⁹⁷ The company is not required to provide any cash to the researcher,⁹⁸ and each party is expected to pay for its own administrative costs.⁹⁹

Each party retains their preexisting patent rights.¹⁰⁰ Ownership of patentable discoveries that arise during the Project will be determined by “inventorship” as currently defined by U.S. patent law,¹⁰¹ meaning whoever conceives the patentable idea will be the inventor or co-inventor.¹⁰² The company has sole discretion about the content of its patent application and where to file.¹⁰³ For jointly-owned patents and patents completely owned by the university, the company will give substantive comments as to the scope of the claims of the patent and will choose where to file the patent applications.¹⁰⁴ In return for this control, the company agrees to pay all application fees, maintenance fees, and opposition fees (such as interference proceedings).¹⁰⁵

The cornerstone of the CRA is found in its provisions for the conclusion of the Project. Once the Project has reached its end point,

97. See, e.g., *id.* § 6.2.

98. See, e.g., *id.*

99. *Id.* There are some costs that must be borne by one of the three entities. For example, the administrative costs of retrieving the pre-clinical data for the drug are solely within the purview of the pharmaceutical company. Likewise, the administrative costs of soliciting, receiving, and analyzing Repurposing Project proposals would fall to the NIH.

100. See, e.g., Janssen CRA, *supra* note 89, § 8.1.

101. See *id.* § 8.2.

102. See *Burroughs Wellcome Co.*, 40 F.3d at 1228 (1994). Based on the oversight capabilities of the PAC and the collaborative nature of drafting the Project Plan, it is most likely that the researcher and a company scientist will be co-inventors. Because conception, rather than reduction to practice, is the “touchstone of inventorship,” it is of no consequence that the researcher will be the one who actually carries out the steps of the research that lead to the method-of-use patent. *Id.* at 1227. Each CRA contains a provision that the university will require its researcher to assign his/her patent rights to it. See, e.g., Pfizer CRA, *supra* note 89, § 8.8. Thus, the company and the university will be the co-owners of any joint-patents.

103. See, e.g., Sanofi CRA, *supra* note 89, § 8.5.

104. For university-owned patents, see, e.g., *id.* § 8.4.1. For jointly-owned patents, see, e.g., *id.* § 8.6.1. Since the company intends to bring the drug to market and is facing potential patent litigation, it is fair to allow it to control the substance of the claims in the patent and where to apply for patent protection.

105. For university-owned patents, see, e.g., Lilly CRA, *supra* note 89, § 7.4.2. For jointly-owned patents, see, e.g., Lilly CRA, *supra* note 89, § 7.6.1. If, in any situation, a party wishes to file in an additional jurisdiction, it may do so at its own expense. If the company decides it will stop developing the drug, it must notify the university that it is planning to let the patent expire. The university has sixty days to decide if it wishes to maintain the patents at its own expense. For university-owned patents, see, e.g., AbbVie CRA, *supra* note 89, § 8.4.2. For jointly-owned patents, see, e.g., AbbVie CRA, *supra* note 89, §§ 8.4.2, 8.6.5.

as defined in the Project Plan, the university will likely own or co-own new patents that will need to be licensed to the company if the latter wishes to pursue FDA approval.¹⁰⁶ The university must negotiate with the original company to grant-back the intellectual property rights it acquired during the collaboration.¹⁰⁷ The company is given the exclusive first option to acquire a “worldwide, royalty-bearing, exclusive or non-exclusive license, including the right to grant sublicenses.”¹⁰⁸ The payment to the university will depend on “the relative contribution of the invention or IND relative to the previous investments made by the company,” as well as the “subsequent investments required to develop a marketed product.”¹⁰⁹ Three of the eight participating companies promote structuring the royalty payment based on a percentage of net sales of the drug (assuming the drug eventually makes it to market).¹¹⁰ As part of the standard CRA, the company will also have the exclusive first option to buy the IND supporting the drug’s continued development.¹¹¹ After the parties agree on terms of the license, the company will use “commercially reasonable efforts” to bring the drug to market.¹¹²

106. Even if further commercial development is not pursued, both parties agree to grant a free license to the other for internal research purposes only. For-profit activities are strictly prohibited under these non-commercial licenses. *See, e.g., AstraZeneca CRA, supra* note 89, §§ 9.1.1 (university to company), 9.1.2 (company to university).

107. *See, e.g., Bristol CRA, supra* note 89, § 9.2.1.

108. *See, e.g., id.* The Lilly CRA, however, does not promise that the license will be royalty-bearing. Instead, the financial terms will be “commercially reasonable.” Lilly CRA, *supra* note 89, § 2.5. The NIH previously recommended using non-exclusive licenses as a means to ensure broader use of the patented technologies. However, it acknowledged that “[t]he determination of when patent protection and exclusive licensing is necessary derives from the specific fact situation attendant the nature of the invention and its market.” *Best Practices for the Licensing of Genomic Inventions: Final Notice*, 70 Fed. Reg. 18413, 18413 (Apr. 11, 2005).

109. Only four of the eight companies incorporated this language into their CRA: AbbVie, AstraZeneca, Bristol, and Janssen. *See, e.g., Bristol CRA, supra* note 89, § 9.2.2. The other four companies use more vague terms such as “commercially reasonable” or “mutually agreeable.” *See, e.g., GlaxoSmithKline CRA, supra* note 89, § 2.5.

110. *See, e.g., Bristol CRA, supra* note 89, § 9.2.2 (“[T]erms shall specifically include, but will not be limited to . . . [percentage of net sales].”). All other companies state that the financial terms will be “commercially reasonable” or “mutually agreeable,” leaving open the possibility that the royalty will be based on net sales, up front royalties, or a combination of the two. *See, e.g., Janssen CRA, supra* note 89, § 9.3.1.

111. *See, e.g., Sanofi CRA, supra* note 89, § 9.2.1.

112. *See, e.g., id.* §§ 9.2.3, 9.3.1.

The two parties have six months to negotiate in good faith the terms of the grant-back license,¹¹³ at which point the discussions will be submitted to a non-binding arbitration proceeding.¹¹⁴ If the two parties cannot reach an agreement, the company maintains its ownership rights in joint-inventions.¹¹⁵ The university will be able to license its rights in joint-inventions to another pharmaceutical company without the project company's permission,¹¹⁶ provided the terms offered to the third party are no better than the terms offered to the original company.¹¹⁷

V. ANALYSIS OF THE REPURPOSING PROJECT AND THE CRAS

A. NCATS and the Repurposing Project are Sound Solutions to the Policy Concerns of the Valley of Death

The NCATS Repurposing Project unites the three key players in biomedical research and development: pharmaceutical companies, university researchers, and the NIH. Each of these entities makes a unique contribution to the Project. Pharmaceutical companies bring knowledge about how to make and use the drug, previous preclinical data about the pharmacokinetics and toxicity of the drug, and the drug itself. University researchers contribute knowledge of the disease target and the manpower to conduct the repurposing research. The NIH has the unique skill of uniting pharmaceutical companies and researchers on a nationwide scale, and it also provides funding for the research. Moreover, the NIH can use its national peer-review process to filter the most promising repurposing proposals. By aligning these three entities, the Repurposing Project creates a triune

113. See, e.g., *id.* § 9.2.3.

114. See, e.g., AstraZeneca CRA, *supra* note 89, § 9.2.3. AbbVie and Sanofi did not include an arbitration clause. See generally AbbVie CRA, *supra* note 89; Sanofi CRA, *supra* note 89.

115. See, e.g., Janssen CRA, *supra* note 89, § 8.6.5; see Lilly CRA, *supra* note 5789, § 7.64; see GlaxoSmithKline CRA, *supra* note 89, § 8.6.4; Pfizer CRA, *supra* note 89, § 8.6.4; Sanofi CRA, *supra* note 89, § 8.6.4.

116. See, e.g., GlaxoSmithKline CRA, *supra* note 89, § 8.6.2.

117. See, e.g., *id.* § 9.2.4. Lilly, Pfizer, and Sanofi do not place this restriction on their university collaborators. See generally, e.g., Lilly CRA, *supra* note 89.

synergy that maximizes the probability of successfully repurposing a drug.

Criticism of the Repurposing Project comes in two major forms. The first argument is that the NIH has improvidently become a drug developer. Under this theory, the Repurposing Project is doomed to fail, because the pharmaceutical companies have already repurposed the drugs that will successfully attain FDA approval, and only the dregs are being thrown to NCATS.¹¹⁸ This argument assumes two points: that accurate predictions can be made about a drug's potential for success, and that pharmaceutical companies are the best entities to make those predictions. Both assumptions are wrong.

The history of the pharmaceutical industry is replete with unexpected failures and long-shot success stories.¹¹⁹ At least twenty-five drugs have been successfully repurposed.¹²⁰ If a drug has been *re*-purposed, that necessarily means that a pharmaceutical company made an incorrect decision about how the drug initially should have been developed. As to the second assumption (that pharmaceutical companies are the best entity to predict a drug's future success), the state of the industry speaks for itself. The old paradigm, in which pharmaceutical companies shouldered sole responsibility for deciding which compounds to develop for FDA approval, led to a logarithmic decrease in the efficiency of biomedical research.¹²¹ Instead of

118. See, e.g., John LaMattina, *The NIH Is Going to Discover Drugs . . . Really?*, FORBES, May 15, 2012, available at <http://www.forbes.com/sites/johnlamattina/2012/05/15/the-nih-is-going-to-discover-drugs-really/>. Dr. LaMattina, echoing the sentiment of Dr. Roy Vagelos, both former executives in big pharmaceutical companies, asked, "Does anyone in the audience believe that there is something that NCATS is going to do that the industry thinks is critical and that they are not doing? That is incredible to think that. If you believe that you believe in fairies." *Id.*

119. The high failure rate of Phase II clinical trials (the trials in which the efficacy of the drug is first tested) proves the limitations in the predictive power of the current preclinical development paradigm. See, e.g., Marion de Jong & Theodosia Maina, *Of Mice and Humans: Are They the Same?—Implications in Cancer Translational Research*, 51 J. NUCL. MED. 501, 501 (2010) ("Differences in size and physiology, as well as variations in the homology of targets between mice and humans, may lead to translational limitations."); Hugo Geerts, *Of Mice and Men: Bridging the Translational Disconnect in CNS Drug Discovery*, 23 CNS DRUGS 915, 915 (2009) ("While animal models have been very useful in documenting the possible pathological mechanisms in many CNS diseases, they are not very predictive in the area of drug development.").

120. See CASE STUDIES, *supra* note 73.

121. See *supra* note 36 and accompanying text.

sequestering universities to basic scientific research and pharmaceutical companies to downstream development, their overlapping expertise should be used synergistically. That is exactly what the Repurposing Project is structured to accomplish.¹²²

Moreover, the pharmaceutical industry has already signaled that it could use the help of university researchers in repurposing drugs. By 2011, several large pharmaceutical companies had begun repurposing collaborations with a single university.¹²³ Making drug repurposing a national endeavor allows bridges to be built between all universities and all pharmaceutical companies.¹²⁴ Indeed, the popularity of the Repurposing Project has exploded with “deluge[s] [of] inquiries from companies large and small offering their compounds.”¹²⁵ The research community has responded with a similar level of interest, as university researchers submitted approximately 160 preliminary project proposals, covering almost every one of the fifty-eight drugs involved in the project.¹²⁶

The second major criticism of the Repurposing Project is that the NIH should be devoting its scarce funds to basic research, as opposed to translational research.¹²⁷ It is certainly true that, given the stagnation and sequestration-driven decline in appropriations,

122. Dr. Collins is cognizant that the NIH should not duplicate the efforts of industry. Rather, he strives for NCATS to “complement—not compete with—translational research at the NIH and elsewhere in the public and private sectors.” Collins, *supra* note 2, at 1.

123. See, e.g., Caroline Arbanas, *Washington University, Pfizer Announce Groundbreaking Research Collaboration*, WASH. U. IN ST. LOUIS NEWSROOM (May 17, 2010), <http://news.wustl.edu/news/Pages/20770.aspx> (Pfizer and Washington University in St. Louis); Kristin Bole, *UCSF, Sanofi Collaborate to Find New Diabetes Cures*, U. CAL. SAN FRANCISCO (Jan. 10, 2012), <http://www.ucsf.edu/news/2012/01/11281/ucsf-sanofi-collaborate-find-new-diabetes-cures> (Sanofi and University of California in San Francisco). Additionally, pharmaceutical companies have struck collaborations with non-profit companies that conduct basic research. See, e.g., Eric Chatelain & Jean-Robert Ioset, *Drug Discovery and Development for Neglected Diseases: the DNDi Model*, 5 *DRUG DESIGN, DEV. & THERAPY* 175, 176 (2011) (GSK, Anacor, Merck, Pfizer, and Novartis collaborating with non-profit R&D group DNDi).

124. This nationalized collaboration was of the scope envisioned by Rai et al. See *supra* notes 85–88 and accompanying text.

125. Mullard, *supra* note 6, at 183.

126. *Id.*

127. See, e.g., David Perrey, *NIH NCATS Drug Repurposing*, CHEM. SPACE (May 16, 2012), <http://chemicalspace.wordpress.com/2012/05/16/nih-ncats-drug-repurposing/> (“[NIH] is there to spur the research, the basic research, that will eventually lead to a practical impact upon society in the form of new treatments, new prevention, or things we can’t yet imagine.”).

budgets are tight at the NIH.¹²⁸ Funding for the NIH has remained under the rate of biomedical research inflation for ten straight years, which has led to a 20 percent decrease in its effective funding power.¹²⁹ Grant applications are awarded funding at a dismal rate of 18 percent.¹³⁰ The funding for NCATS and the Repurposing Project, however, is negligible in comparison to the NIH's total budget. The NIH grants \$24.7 billion annually to university researchers.¹³¹ By contrast, approximately \$20 million is expected to be granted through the Repurposing Project each year.¹³² This constitutes *less than one-tenth of one percent* of the NIH's total spending. Allocating these funds to basic research would have little to no overall effect on the total amount devoted to the basic research sector.

When budget constraints are tight, the most efficient therapeutic projects, with higher likelihoods of resulting in FDA approval, should receive public funding. The Repurposing Project fits that description. Repurposing a drug that is already bolstered by preclinical data and early human safety data has a higher likelihood of resulting in an FDA-approved drug. Basic exploratory research, even when successful, still has to clear the Valley of Death and navigate the gauntlet of clinical trials before reaching patients.¹³³ Moreover, biomedical research occurs across the entire timeline of drug development, and the NIH has traditionally funded both basic and

128. At the meeting for the NIH Advisory Committee, Francis Collins stated, "These are trying times . . . historically difficult times. . . . The final numbers for FY 2012 are indeed sobering . . . and a deep source of concern." *Budget Concerns Voiced at Director's Advisory Committee*, NAT'L INST. HEALTH (July 8, 2011), http://nihrecord.od.nih.gov/newsletters/2011/07_08_2011/story3.htm. In fact, the United States decreased its total spending on biomedical research from 2007–2012, both in public and private expenditures. Chakma et al., *supra* note 11, at 5.

129. Jocelyn Kaiser, *A Flat Budget for NIH in 2013*, SCI. INSIDER (Feb. 13, 2012), <http://news.sciencemag.org/scienceinsider/2012/02/a-flat-budget-for-nih-in-2013.html>.

130. *Id.*

131. This is 80 percent of the NIH's total budget of \$30.9 billion. *NIH Budget*, NAT'L INST. HEALTH, <http://www.nih.gov/about/budget.htm> (last visited Feb. 8, 2013).

132. *Discovering New Therapeutic Uses for Existing Molecules: A Pilot NIH-Industry Program*, NAT'L CENT. ADVANCING TRANSLATIONAL MED., at 1, <http://www.ncats.nih.gov/research/reengineering/rescue-repurpose/therapeutic-uses/funding.html> (last visited Nov. 5, 2013). In its first round of funding, only \$12.7 million was granted. *New Therapeutic Uses Funding Information*, NAT'L INST. HEALTH, <http://www.ncats.nih.gov/research/reengineering/rescue-repurpose/therapeutic-uses/funding.html> (last visited Feb. 8, 2013).

133. See *supra* Part II.A–B.

applied research.¹³⁴ Thus, it is well within NIH's purview to fund research projects that have a high likelihood of translating into successful therapeutics for patients. The shortage of funding for basic research, which is a very real and pressing concern, is better solved by Congress increasing the NIH's total budget, rather than misdirecting funds from translational research like the Repurposing Project.

B. The CRAs Effectively Address Concerns about Patent Ownership and Allocation of Costs and Resources

The CRAs efficiently facilitate a collaborative relationship between the pharmaceutical company, the university researcher, and the NIH. The two potential sources of friction discussed in Part III, above, have been effectively dealt with *ex-ante* in these agreements. The first concern, the allocation of IP ownership rights to inventions arising during the project, is handled by allowing the university researcher to retain ownership of IP if he or she conceived of the innovation. This is consistent with current patent law. At the conclusion of the Project, the university will either sell those IP rights back to the original company or to a third party. In either case, the university is rewarded financially for its innovative contribution.

The second concern, fairly distributing risks, costs, and potential profits amongst the participants, is also effectively addressed and evenly balanced in the Project. In terms of cost, each party is donating significant resources to the Project. The NIH granted \$12.7 million for nine projects in 2013.¹³⁵ The university is contributing the manpower to conduct the research and complete the required regulatory procedures. The company is opening up its medicine cabinet to allow outsiders access to a drug that is patent-protected and bolstered by positive results from some previous experiments. The risk accompanying further development and the dispersal of potential

134. "NIH's funding for basic research is slightly over half (54 percent) of research funding, and this balance between basic and applied research has remained fairly constant over the past decade." FRANCIS COLLINS, NAT'L INST. HEALTH, TESTIMONY BEFORE THE HOUSE SUBCOMM. ON LABOR—HHS—EDUC. APPROPRIATIONS 4–5 (Mar. 20, 2012), *available at* http://www.nih.gov/about/director/budgetrequest/fy2013_testimony_house.pdf.

135. *NIH to Fund Collaborations*, *supra* note 6.

rewards are contemplated in the royalty payments of the option license. The promise that payments to the university will consider “the relative contribution of the invention or IND relative to the previous investments made by the company” and the “subsequent investments required to develop a marketed product” perfectly balances the costs, risks, and rewards to the participants.¹³⁶

The CRAs also require the university to negotiate with the pharmaceutical company first if it attempts to sell any patent or IND originating from the Repurposing Project.¹³⁷ This might raise antitrust concerns,¹³⁸ but the terms of the CRAs are not manifestly anticompetitive. The CRAs do not require the pharmaceutical company to purchase the grant-back license. Rather, the university researcher merely presents the company with the option to do so. If these negotiations fail, then, under the terms of the CRA, the university researcher has the right to license the IP to a third party without the original company’s consent.¹³⁹ Furthermore, the purpose of this exclusive option is to decrease the risk that a pharmaceutical company’s patented products and underlying trade secrets will be shared with outside researchers. Thus, the provision incentivizes risk-averse companies to participate in the Repurposing Project, leading to collaboration and the development of therapies. Protections for relationship-specific investments are typically weighed by the courts

136. See *supra* note 109 and accompanying text. Although the four companies that do not include this specific language make vague promises to be “reasonable” or “agreeable,” *supra* note 109, they should consider using this language. It is a strong signal to potential collaborators and policymakers that the companies will consider the proper factors when negotiating the terms of the grant-back license.

137. See *supra* notes 107–08 and accompanying text.

138. See, e.g., Mueller, *supra* note 80, at 59–62 (arguing that reach-through royalties for mandatory licenses of basic research tools are per se valid if the royalty payment does not exceed the life of the underlying patent). The antitrust concerns discussed by Mueller are even less relevant in this context, because the underlying patent involves a product that is further downstream in the development process. Mueller, as well as several other commentators on biomedical research policy, focuses on issues arising from the fact that patents protecting basic research tools may stifle innovation. See, e.g., Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698 (1998); Rai & Eisenberg, *supra* note 60. While their concerns are relevant to those situations, they do not apply to the Repurposing Project, where the patents at issue are much further downstream as they involve a drug or a method of using a drug to treat a disease.

139. See *supra* notes 113–17 and accompanying text.

in determining if a business practice is unfairly anticompetitive.¹⁴⁰ In this context, the first option provision is best understood as an incentive to collaborate, rather than being manifestly anticompetitive. Thus, it does not amount to an antitrust violation.¹⁴¹

VI. CONCLUSION

The Repurposing Project pragmatically builds bridges across the Valley of Death. Aligning pharmaceutical companies, university researchers, and the NIH promotes a triune synergy unique to the biomedical research field. Without any one of these three entities, the Project would lack an important element that is necessary for its success. University researchers bring important knowledge about the new disease to be targeted. Pharmaceutical companies supply know-how about using the drug and valuable data that can support an IND. The NIH provides a nationwide infrastructure for uniting researchers with companies and for selecting the most promising repurposing proposals.

Most importantly, the launch of NCATS and the Repurposing Project advances the mission statement of the NIH: “to enhance health, lengthen life, and reduce illness and disability.”¹⁴² Repurposing abandoned drugs fills an important gap in biomedical

140. *See, e.g.,* Cont’l T.V., Inc. v. GTE Sylvania, Inc., 433 U.S. 36, 37 (1977) (holding sales restriction used by respondent should be judged under the traditional rule-of-reason standard).

141. A related challenge could be brought against the grant-back licenses in the Repurposing Project under the patent law doctrine of patent misuse. This equitable defense to patent infringement prohibits the patentee from “extend[ing] the economic effect beyond the scope of the patent grant.” *C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1372 (Fed. Cir. 1998) (citing *Mallinckrodt, Inc. v. Medipart, Inc.*, 976 F.2d 700, 703–04 (Fed. Cir. 1992)). Patent misuse “requires that the alleged infringer show that the patentee has impermissibly broadened the ‘physical or temporal scope’ of the patent grant with anticompetitive effect.” *Virginia Panel Corp. v. MAC Panel Co.*, 133 F.3d 860, 868 (Fed. Cir. 1997) (quoting *Windsurfing Int’l, Inc. v. AMF, Inc.*, 782 F.2d 995, 1001 (Fed. Cir. 1986)). The licenses in the Repurposing Project should survive any attack under the patent misuse doctrine. Courts typically give broad latitude to the terms of a license negotiated in good faith by the parties. *See, e.g.,* *Bayer AG v. Housey Pharms.*, 228 F. Supp. 2d 467 (D. Del. 2002) (holding that a license with reach-through royalty provisions that extended even beyond the temporal scope of the patent was not per se invalid because the license was not conditioned upon the acceptance of that term). Moreover, the terms of the grant-back licenses in the Repurposing Project are unlikely to be deemed anticompetitive. *See supra* notes 138–40 and accompanying text.

142. *See supra* note 58.

research. Despite criticism,¹⁴³ the pharmaceutical industry is not commandeering university researchers. Rather, the pharmaceutical industry is collaborating with researchers and paying them a percentage of the profits realized from a successfully developed drug. The Repurposing Project provides another way to conceptualize translational medicine—sharing capital (monetary and intellectual) amongst drug sellers and basic researchers. Far from overstepping its bounds, NCATS is a pragmatic and efficient mechanism for creating synergy in biomedical research to benefit human health.

143. *See supra* note 118.